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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/326,402	06/04/1999	MARTA BLUMENFELD	GENSET.030A	4132

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EXAMINER	
MAHATAN, CHANNING	
ART UNIT	**PAPER NUMBER**
1631	26

DATE MAILED: 08/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/326,402	BLUMENFELD ET AL.	
	Examiner	Art Unit	
	Channing S. Mahatan	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-182* is/are pending in the application.

4a) Of the above claim(s) *89-120, 142-149, and 153-162* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *121-141,150-152 and 163-182* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *89-182* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Attachment for PTO-948* .

DETAILED ACTION

APPLICANTS' ELECTION

Applicants' election with traverse of SEQ ID NO: 12 (single polymorphic site at position 402) in Paper No. 25, filed 11 March 2002, is acknowledged. It is acknowledged that the restriction requirement mailed 18 April 2001, Paper No. 15, did not require an election of a particular species of generic SEQ ID. No. 12. However, the search of more than one species (polymorphic site) would result in an undue search burden since each site is distinctly different within the sequence constituting independent and distinct inventions. At present the huge number of submissions of claims directed to various sequences, such as nucleic acids or polypeptides, is so large that the election of one (1) sequence (and one (1) polymorphic site, in the pending application) of this type is now deemed to be practically appropriate so as not to overwhelm the examination and search processes for such claims. Thus, the traversal argument that "rejoinder of the inventions would not create an undue search or examination burden on the Examiner or the Patent Office" is found unpersuasive. Further, it is acknowledged that SEQ ID NO: 12 contains the appropriate symbols corresponding to the election of Paper No. 18, filed 22 June 2001 (SEQ ID NO: 1). Claims 89-120, 142-149, and 153-162 remain withdrawn as not directed to the elected subject matter and all sequences other than the elected SEQ ID. NO. 12 are withdrawn.

APPLICANTS' ARGUMENTS

Applicants' arguments in Paper No. 13, filed 26 February 2001, have been fully considered but they are not deemed to be persuasive for the reasons set forth below. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The

following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

OBJECTION BY DRAFTSMAN

Applicants are hereby notified that the required timing for correction of drawings has changed. See the last 6 lines on the sheet, which is attached, entitled "Attachment for PTO-948 (Rev. 03/01 or earlier)". Due to the above notification Applicant is required to submit drawing corrections with the time period set for responding to this Office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

SEQUENCE COMPLIANCE

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a) (1) and (a) (2). This application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825 due to the sequences in Figures 7A-D, and no submission of the following items. Therefore, applicants are required to submit the following:

1. As a separate part of the disclosure on paper copy or compact disk copy, a "Sequence Listing" as 37 C.F.R. § 1.821(c).

2. A copy of the "Sequence Listing" in computer readable form as required by 37 C.F.R. § 1.821 (e).

3. A statement that the content of the paper and computer readable copies are the same and include no new matter, as required by 37 C.F.R. § 1.821 (f) and 37 C.F.R. § 1.821 (g).

4. Each sequence in the specification is required to have a SEQ ID NO. therewith. It should be noted that SEQ ID NOs. are not required in the Figures per se, but may be set forth in the Brief Description of the Drawings section.

Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action. A complete response to this office action includes compliance with this sequence rule compliance requirement. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this office action.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 121-141, 150-152, 163-182, and SEQ ID NO: 12 (position 402).

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

SCOPE OF ENABLEMENT

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 U.S.P.Q. 546 (B.P.A.I. 1986) and reiterated by the Court of Appeals in In re Wands, 8 U.S.P.Q.2d 1400 at 1404 (C.A.F.C. 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Claims 121-141, 150-152, and 163-182 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying a nucleotide (species position 67092 of the elected SEQ ID NO: 12) at a PCTA-1 biallelic marker (A30, allele T) in sporadic prostate cancer, does not reasonably provide enablement for the identification of other nucleotides at other PCTA-1 biallelic markers in familial (i.e. A2, A41, etc) or sporadic (i.e. A2, A30, etc.) prostate cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. It is noted that applicants have disclosed that significant p values are preferably less than .01, (page 110, lines 6-13 of the Specification).

The following statistical/numerical values are derived from Table 5 (Haplotype frequency analysis for the familial cases of prostate cancer):

	A2(A)	A30(T)	A41(T)	A55(C)	A57(G)	A75(G)
frequency % (case/control)	67/67	72/66	75/71	72/68	72/69	95/95
p value	0.75	0.033	0.14	0.20	0.25	0.75

The analysis of Table 5 reveals that only biallelic marker A30 (position 67092, allele T) has a case frequency % greater than the control frequency % (noted to be 6%) and a statistically

significant p value (0.033). All other biallelic markers A2 (position 402, allele A), A41 (position 68525, allele T), A55 (position 82234, allele C), A57 (position 82393, allele G), and A75 (position 87713, allele G) have statistically insignificant p values, thus displaying no correlation between said biallelic markers and familial cases of prostate cancer.

The following statistical/numerical values are derived from Table 6 (Haplotype frequency analysis for the sporadic cases of prostate cancer):

	A2(A)	A30(T)	A41(T)	A55(C)	A57(G)	A75(G)
frequency % (case/control)	60/67	64/66	73/71	64/68	65/69	94/95
p value	0.0077	0.43	0.29	0.16	0.14	0.34

It is acknowledged that the biallelic marker A2 (allele A) has a statistically significant p value (0.0077), however, the sporadic case frequency % is less than the control frequency % (noted to be 7%). Thus, it is unclear how the A2 (allele A) biallelic marker can be utilized to detect sporadic cases of prostate cancer given that the marker is incapable of distinguishing between case (sporadic prostate cancer) and control population (based on frequency %). Further, all other biallelic markers A30 (allele T), A41 (allele T), A55 (allele C), A57 (allele G), and A75 (allele G) have statistically insignificant p values (less than 0.05), thus displaying no correlation between said biallelic markers and sporadic cases of prostate cancer.

Applicants have failed to disclosed correlative data relating to other biallelic markers (markers not disclosed in Tables 5 and 6), thus non-enabling. The statistically insignificant p values and frequency % (A2 (allele A) sporadic prostate cancer) for biallelic markers A2 (allele A), A30 (allele T), A41 (allele T), A55 (allele C), A57 (allele G), and A75 (allele G) are

unpredictable in the method of identifying a nucleotide at a PCTA-1 biallelic marker in familial (not A30; allele T) and sporadic prostate cancer; requiring further direction and undue experimentation.

LACK OF WRITTEN DESCRIPTION

Claims 121-141, 150-152, and 163-182 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO: 12, which corresponds in some way to a cDNA encoding a related PCTA-1 gene. SEQ ID NO: 12 per se meets the written description and enablement provisions of 35 U.S.C. § 112, first paragraph. However, claims 121, 140, 151, 152, 167-172, 177, and 178 are directed to encompass gene sequences, and fragments (see below 112 2nd Paragraph Rejection; Vague and Indefinite section) of sequences of SEQ ID NO: 12, corresponding sequences from other species, mutated fragment sequences, allelic variants, splice variants, and so forth. None of these additional sequences meet the written description provision of 35 U.S.C. § 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. This is a rejection based on a lack of WRITTEN DESCRIPTION.

> Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO. 12; the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides (i.e. complements), regardless of the

complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 U.S.P.Q.2d 1601, 1606 (C.A.F.C. 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 U.S.P.Q.2d 1016. In Fiddes v. Baird, 30 U.S.P.Q.2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 U.S.P.Q.2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only SEQ ID NO: 12 but not the full breadth of the claims meets the written description provision of 35 U.S.C. § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that

Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision. (See page 1115.)

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 121-141, 150-152, and 163-182 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

VAGUE AND INDEFINITE

Claims 121, 140, 151, 152, 167-172, 177, 178, and all claims dependent therefrom are vague and indefinite as to what is meant therein by the limitation "the complement". A possible interpretation is that the complement must be of the same length and be the full and exact complement of the recited SEQ ID NO. sequence. Another interpretation is that any complement is meant including those with less than 100% complementarity, such as 90%, 50%, or even 10%. Clarification of the metes and bounds of the claim is requested via clearer claim wording.

Claims 121 (line 2), 131 (line 1), 132 (lines 3 and 5), 133 (line 3), 150 (line 3), 151 (line 1), 152 (line 1), 167 (line 1), 168 (line 1), 169 (line 1), 170 (line 1), 171 (line 1), 172 (line 1), 177 (lines 1 and 2), 178 (lines 1 and 2), and all claims dependent therefrom are vague and indefinite as to what is meant therein by the limitation "PCTA-1-related biallelic marker". It is unclear by what the limitation applicants' are referring to as "related". "Related" implies some degree/criteria of relatedness. Thus, applicants can resolve this issue by particularly pointing out the metes and bounds of "related", via clearer claim language.

Claims 150 (lines 1-2) and all claims dependent therefrom are indefinite due to the lack of clarity of the claim language failing to recite a final process step, which agrees back with the preamble. The preamble states that it is "a method of determining whether an individual is at risk of developing prostate cancer", however the claim recites a final step of correlating the result of the step a) with a risk of developing prostate cancer. The claim does not set forth the conditions/state when in any of the claim steps that such "risk is determined". While minor details are not required in method/process claims, at least the basic step must be recited in a positive, active fashion. Clarification of the metes and bounds of the claim is requested via clearer claim wording.

LACK OF ANTECEDENT BASIS

Claim 140 (line 2) recites the phrase "control population" which lacks antecedent basis from claim 132. It is acknowledged that claim 132 (line 5) recites "control", however lacks any indication that said control is a "control population".

Claim 141 (line 1) recites the phrase "case control population" which lacks antecedent basis. Again it is acknowledged that claim 1332 (line 5) recites "control", however lacks any indication that said control is a " case control population.

OBJECTION OF DISCLOSURE

The disclosure is objected to because of the following informalities:

The disclosure is objected to because of the confusion which exists between elected SEQ ID NO: 12 and SEQ ID NO: 1. As stated above it is acknowledged that SEQ ID NO: 12 contains the appropriate symbols corresponding to the election of Paper No. 18, filed 22 June 2001 (SEQ ID NO: 1), however, the current specification does not make any indication that SEQ ID NO: 12

is the same as SEQ ID NO: 1. Applicants' are required to amend the specification to remove the confusion; i.e. substituting "SEQ ID NO: 12" for "SEQ ID NO: 1".

The disclosure is objected to because of a confusing paragraph structure (page 190, lines 19-21) and/or correlation to Tables 5 or 6. Applicants' disclose "a strong association between the allele A of the biallelic marker and sporadic prostate cancer"; however fail to denote the position of allele A. Applicants' denote the p value of said association to be 7.71×10^{-3} supported by Table 6 (Haplotype frequency analysis for the sporadic cases of prostate cancer), however, only showing allele T of the A2 biallelic marker. It is noted that Table 5 (Haplotype frequency analysis for the familial cases of prostate cancer) displays the allele A of the A2 biallelic marker, however, with a p value of 7.5×10^{-1}. Such confusing paragraph structure and correlation to tables requires correction.

The disclosure is objected to because it contains an embedded hyperlink and/or other forms of browser-executable code and delete them on page 172, line 3. Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See M.P.E.P. § 608.01 and § 608.01(p). The current format utilized by applicants is executable, therefore, a suggested reference format for the said hyperlink objection is "World Wide Web address: gcg.com".

Appropriate Correction Is Required.

No Claims Are Allowed.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Channing S. Mahatan whose telephone number is (703) 308-2380. The examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, William Phillips, whose telephone number is (703) 305-3482 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Date: August 21, 2002

Examiner Initials: CSM

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER